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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,409	12/28/2001	Masahiro Iwakura	04853.0084	3873
22852	7590	05/04/2004	EXAMINER	
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 1300 I STREET, NW WASHINGTON, DC 20005			PROUTY, REBECCA E	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/019,409	<b>Applicant(s)</b> IWAKURA, MASAHIRO	
	<b>Examiner</b> Rebecca E. Prouty	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 27 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 1-6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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Claims 1-10 are still at issue and are present for examination.

Claims 1-6 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicants' arguments filed on 1/27/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim 7-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of construction the sulfur-free DHFR genes of Table 7 of the specification and a sulfur-free xylanase gene encoding SEQ ID NO:9, does not reasonably provide enablement for methods of constructing any sulfur-free enzyme having activity greater than or equal to the activity of the original protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The rejection was explained in the previous Office Action.

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Applicants argue that because the claimed methods include a step of "selecting a sulfur atom-free enzyme protein having activity greater than or equivalent to that of the original enzyme protein" that the rejection is improper and the claims enabled. This is not persuasive, as the specification fails to provide a reasonable expectation that this step is possible for **any** enzyme in which every methionine and cysteine codon has been substituted. The showing of success in two particular enzymes (both of lack any cysteine residues at all at the start and have only a small number of residues) fails to provide an expectation that this can be accomplished in all other enzymes. The number of sulfur-containing amino acids as well as the importance of each of them for the particular enzymatic activity of each enzyme, is highly unpredictable and varies widely. As such while one clearly could mutate each sulfur containing amino acid in an enzyme of interest and could test the enzymatic activity of each of the resulting mutants using the methods claims, one would not have any predictability as to whether **any** of the mutants screened in the final step would in fact have an activity greater than or equivalent to that of the original enzyme protein. As such the skilled artisan would not know which enzymes the disclosed methods would be applicable to and

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the specification, fails to provide any guidance for selecting those enzymes that could be reasonably expected to succeed.

Applicants appear to argue that the specification shows an example of the mutation of an enzyme that naturally includes cysteine residues as *E. coli* DHFR includes two cysteine residues. This is not persuasive because as above, the showing of success for one enzyme, provides no predictability with regard to success of mutating other enzymes as well.

Furthermore, even for the instant case of *E. coli* DHFR, the prior art had previously shown that a cysteine free version of the enzyme had enzymatic activity. For the vast majority of enzymes, however, there is no such showing and the importance of cysteine residues in the catalytic activity of many enzymes is well known in the art.

The rejection of Claims 7-10 under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Li et al. and Recktenwald et al., in view of Lathrop et al. and Barnett et al. (WO96/30481) is withdrawn in view of applicants arguments the rejection is inconsistent with the examiner arguments regarding a reasonable expectation of success of obtaining an mutant enzyme having a activity equal or greater to the activity of the unmodified enzyme when all cysteine and methionine

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residues are modified in the above 112, first paragraph.

However, applicants should note that arguments by applicants that **the prior art** provides such reasonable expectation will be used in combination with the above references to reinstate the 103 rejection as the disclosed prior art clearly suggests and motivates the skilled artisan to try such modifications and teaches all portions of applicants claimed methods for doing so as previously explained.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

A handwritten signature in black ink, appearing to read 'Rebecca Prouty', with a stylized flourish at the end.

Rebecca Prouty  
Primary Examiner  
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